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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,346	12/02/2003	Teresa Mujica-Fernaud	MERCK-2808	1373

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EXAMINER	
ISSAC, ROY P	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,346	MUJICA-FERNAUD ET AL.	
	Examiner	Art Unit	
	Roy P. Issac	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *8-21,24-27 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,22,23,28,29 and 31-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application claims priority under 35 U.S.C §119 (a)-(d) and 365(c) to foreign application Germany 10256182.6 filed 12/02/2002. The copy of certified copy of the priority has been filed with the instant Application. It is noted that no English translation of said Germany application has been provided.

Election/Restrictions

Applicant's election with traverse of the invention of Group I, claims 1-7, 22-23, 28-29, 31-32 and 33-34 in the reply filed 03 November 2006 is acknowledged.

The traversal is on the grounds that there exists a sub-combination, combination relationship between inventions of Group I and Group II. Applicants' argument was found unpersuasive since inventions of group I, and group II belong to different statutory classes of inventions. Invention of Group I relates to product claims while invention of Group II relates to process of using. The requirements for restriction between product claims and process claims is well established, as set forth in the previous office action. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the processes as claimed can be practiced with another materially different product.

Furthermore, the search for inventions of groups I and II will place an undue burden on the Office. The search field for compositions is non-coextensive with the search field for a process of using the same compositions. A reference to the compositions herein would not necessarily be a reference to the method of using the same herein. The compositions and methods of use have separate consideration as to patentability.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above

policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The restriction requirement between Inventions I and II was deemed proper and is therefore made FINAL.

Claims 8-21, 24-27 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction requirement in the reply filed on 03 November 2006.

Claims 1-7, 22-23, 28-29, 31-32 and 33-34 will be examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 22-23, 28-29 and 31-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds 6-hydroxy-2-[3-(4-tert-butylphenyl)-1,2,4-oxadiazol-5-yl]chromone, 7-hydroxy-2-[3-(4-tert-butylphenyl)-1,2,4-oxadiazol-5-yl]chromone, and 6-hydroxy-2-[3-(pyridin-2-

yl)-1,2,4-oxadiazol-5-yl]chromone, does not reasonably provide enablement for all of the thousands of molecules encompassed by the generic formula I-VII. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant application relates to 2-Oxadiazolechromone and the process for synthesizing the same.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a PhD, M.S. or equivalent advanced degree.

The breadth of the claims:

The claims of the instant application are deemed broad because the generic formulae I-VII encompasses thousands of molecules wide varying functionalities. The plethora of functional groups described as substituents for said generic claims encompass a significant portion of all known organic functionalities and many have divergent properties.

The presence or absence of working examples and the amount of direction or guidance presented:

Examples 1 and 2 describes the synthesis of compounds, 6-hydroxy-2-[3-(4-tert-butylphenyl)-1,2,4-oxadiazol-5-yl]chromone, 7-hydroxy-2-[3-(4-tert-butylphenyl)-1,2,4-oxadiazol-5-yl]chromone, and 6-hydroxy-2-[3-(pyridin-2-yl)-1,2,4-oxadiazol-5-yl]chromone. Other examples in the specification describes the preparation of injection vials, suppositories, solution formation, ointment, tablets, coated tablets, capsules and ampoules.

There are no examples wherein the X is OA, phenoxy, Ar, O-CO-A, SO3H, SO3A, OSO3A, OSO3H, SO2A, Hal, COOH, COOA, CONH2, NHSO2A, COA, CHO or SO2NH2. There are no examples of synthesis where OH or Hal. Furthermore, there are no examples of any asymmetric synthesis or isolation of any chirally pure products from racemic mixtures. Furthermore, the separation of racemic mixtures to obtain chirally pure products requires trial and error experimentation by skilled organic chemists. The development of experimental methods to encompass chiral separation is by far a trial and error process. (Montanari et. al. Journal of Chromatography, 1121, 2006, 64-75; PTO-892,

Cited by the examiner). The development of useful chiral methods challenges the pharmaceutical industry. (Page 74, Column 1, Conclusions). The prediction of chiral stationary phase would be the most appropriate to separate chiral drugs is not an easy task as it involves a wide range of complex components. (Conclusions). The screening methods are not sufficient to characterize adequately the chiral retention mechanisms because there is no single interaction capable of explaining chiral separation and recognition. (Conclusions). Thus, one of skill in the art will have undertake significant research activities to obtain isolated stereoisomers as claimed herein.

The lack of working examples is a critical and crucial factor to be considered, especially in cases involving an unpredicatable and undeveloped art. See MPEP § 2164.

The predictability or lack thereof in the art and The quantity of experimentation necessary

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that the recitation encompasses thousands of compositions with varying effects and unknown side effects. As such, each composition will need to be individually evaluated for activity.

Organic synthesis in particular is very unpredictable. Some of the synthesis efforts in organic chemistry take years to complete, often an exercise in trial and error. The generic claims in the instant application encompass thousands of compounds with wide varying functional groups. The additional groups claimed by the generic formula have well-established divergent function and properties. For example, the fluorinated compounds are well known in art as having divergent properties than the straight chain alkyl groups of the instant invention. (PTO-892; Cited by the examiner; Dave R., et. al. Amino Acids, 24, 2003, 245-261). Dave et. al. notes that, "It is well recognized that replacing a hydrogen atom by a fluorine atom in a chemical entity can bring significant changes in its chemical and biochemical behaviour." (Page 245, Column 2, lines 5-10). In the same vein, one of ordinary skill in the art will recognize that substituents with oxygen, sulfur, and nitrogen will substantially change the nature of the compounds as well the methodology required to synthesize them.

In the instant case, some of the claimed functional substituents are incompatible with the synthetic strategy claimed. For example, if X is COOH or CHO, it is very likely that the reaction claimed will not lead to the compound of generic formula I.

Thus, the specification fails to provide clear and convincing evidence in sufficient support of the claimed compounds in their full scope represented by the generic formulae I-VII and the process for making the same.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful

conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the *Wands* factors as discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in ***undue experimentation*** to practice the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation "additional pharmaceutically active compound" renders the claim indefinite. The phrase is not clearly defined in the specification and the phrase does not clearly delineate any specific compounds or group of compounds. As such, one of skill in the art would not be apprised of the metes and bounds of the claims herein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Tronche et. al. (U.S. Patent No. 3,816,470; PTO-892, Cited by the examiner).

Tronche et. al. discloses chromone-carboxylic-2 acid chloride, a compound that reads on the generic formula VI. (Column 6, lines 67-72).

Claim 33 is rejected under 35 U.S.C. 102(b) as being anticipated by Augestein, J et. al. (BP 1,447,480; PTO-892, Cited by the examiner). Augestein discloses acid halides of the instant application in the synthesis of chromone carboxyamido tetrazoles. (Page 18, lines 15-23; claim 6).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Roy P. Issac whose telephone number is 571-272-2674. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12/20/06

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